

AMENDMENTS TO THE CLAIMS

1-12. (canceled)

13. (currently amended) A 38-residue or 39-residue CRF cyclic peptide, or a nontoxic salt thereof, which binds to CRFR1 with an affinity substantially greater than it binds to CRFR2, which peptide has the following formula:

$$Y_1\text{-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-R}_{14}\text{-R}_{15}\text{-Arg-R}_{17}\text{-R}_{18}\text{-R}_{19}\text{-Glu-Nle-Ala-Arg-Ala-Glu-Gln-R}_{27}\text{-Ala-Gln-Gln-Glu-R}_{32}\text{-R}_{33}\text{-Lys-Arg-R}_{36}\text{-R}_{37}\text{-Nle-Glu-R}_{40}\text{-R}_{41}\text{-NH}_2$$

wherein the sidechains of Glu and Lys indicated are covalently linked; Y_1 is an acyl group having not more than 15 carbon atoms or is radioiodinated tyrosine; R_{14} is CML or Leu; R_{15} is CML or Leu; R_{17} is Glu or CML; R_{18} is Val or CML; R_{19} is CML or Leu; R_{27} is CML or Leu; R_{32} is His or D-His; R_{33} is Aib, D-Ala, D-Ser or Ser; R_{36} is Lys or CML; R_{37} is CML or Leu; R_{40} is Ile or CML; and R_{41} is Ile or CML; provided that ~~a cyclizing bond exists between Glu in position 31 and Lys in position 34 and provided further that~~ D- β -(2-naphthyl)alanine(D-2Nal) or D-Leu may be substituted for D-Phe.

14. (currently amended) A CRF agonist peptide, or a nontoxic salt thereof, which binds to CRFR1 with an affinity substantially greater than it binds to CRFR2, which peptide has the following formula:

~~(cycle 31-34)~~ $Y_1\text{-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-Leu-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu-Nle-Glu-Ile-Ile-NH}_2$, wherein Y_1 is an acyl group having not more than 7 carbon atoms or is radioiodinated tyrosine, and wherein a cyclizing bond may exist between the side chains of Glu ~~in the 31-position~~ and Lys ~~in the 34-position~~ as indicated.

15. (currently amended) A 38-residue or 39-residue CRFR1 ligand cyclic peptide which binds to CRFR1 with an affinity substantially greater than it binds to CRFR2, which peptide has the following formula, or a nontoxic salt thereof:

(eyele 31-34)Y₁-Pro-Pro-R₆-Ser-R₈-Asp-Leu-R₁₁-D-Phe-His-R₁₄-R₁₅-Arg-Glu-R₁₈-Leu-R₂₀-Nle-R₂₂-R₂₃-Ala-R₂₅-Gln-R₂₇-Ala-R₂₉-Gln-Glu-R₃₂-R₃₃-R₃₄-Arg-R₃₆-R₃₇-Nle-R₃₉-R₄₀-R₄₁-NH₂ wherein the side chains of Glu and R₃₄ are covalently linked as indicated; Y₁ is an acyl group having not more than 7 carbon atoms or is radioiodinated tyrosine; R₆ is Ile, Met or Nle; R₈ is Leu or Ile; R₁₁ is Thr or Ser; R₁₄ is CML or Leu; R₁₅ is Leu or CML; R₁₈ is Val, CML, Nle or Met; R₂₀ is Glu or D-Glu; R₂₂ is Ala or Thr; R₂₃ is Arg or Lys; R₂₅ is Asp or Glu; R₂₇ is Leu or CML; R₂₉ is Gln or Glu; R₃₂ is His, Aib, Ala, Gly, Leu, Gln or Glu; R₃₃ is Aib or an L- or D-isomer of Ser, Asn, Leu, Ala, CML or Ile; R₃₄ is Lys or Orn; R₃₆ is Lys or Leu; R₃₇ is CML or Leu; R₃₉ is Glu or Asp; R₄₀ is Ile, CML or Glu; and R₄₁ is Ala, Aib or Ile; provided that D-β-(2-naphthyl)alanine(D-2Nal) or D-Leu may be substituted for D-Phe.

16. (new) A CRF cyclic peptide according to claim 15 having the formula:
Y₁-Pro-Pro-R₆-Ser-R₈-Asp-Leu-R₁₁-D-Phe-His-R₁₄-Leu-Arg-Glu-R₁₈-Leu-R₂₀-Nle-R₂₂-R₂₃-Ala-R₂₅-Gln-Leu-Ala-R₂₉-Gln-Glu-R₃₂-R₃₃-R₃₄-Arg-R₃₆-R₃₇-Nle-R₃₉-R₄₀-R₄₁-NH₂ wherein Y₁ is an acyl group having not more than 7 carbon atoms; R₂₀ is Glu or D-Glu; R₂₂ is Ala or Thr; R₂₃ is Arg or Lys; R₂₉ is Gln or Glu; R₃₂ is His, Aib or Ala; R₃₆ is Lys or Leu; R₃₇ is Leu or CML; R₃₉ is Glu or Asp; R₄₀ is Ile, CML or Glu; and R₄₁ is Ile, Aib or Ala; wherein the remaining variables are as defined in claim 15.

17. (new) A peptide according to claim 15 wherein R₁₈ is Val, R₂₂ is Ala, R₂₃ is Arg, R₂₅ is Glu, R₃₉ is Glu, and R₄₁ is Ile.

18. (new) A peptide according to claim 15 having the following formula, or a nontoxic salt thereof:

Y₁-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-R₂₂-R₂₃-Ala-Glu-Gln-R₂₇-Ala-Gln-Gln-Glu-R₃₂-R₃₃-Lys-Arg-Lys-Leu-Nle-Glu-R₄₀-Ile-NH₂ wherein Y₁ is an acyl group having not more than 7 carbon atoms; R₂₂ is Ala or Thr;

R₂₃ is Arg or Lys; R₂₇ is Leu or CML; R₃₂ is His; R₃₃ is Ser or Aib; and R₄₀ is Ile or CML.

19. (new) A peptide according to claim 13 having the formula:

Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val- Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-Leu-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu- Nle-Glu-Ile-Ile-NH₂, or

Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val- Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-CML-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys- Leu-Nle-Glu-Ile-CML-NH₂; or

Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val- Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-CML-Ala-Gln-Gln-Glu-His-Aib-Lys-Arg-Lys- Leu-Nle-Glu-Ile-CML-NH₂.

20. (new) A peptide according to claim 13 having the formula:

Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-CML-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-Leu-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu- Nle-Glu-Ile-Ile-NH₂, or

Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-CML-Leu-Arg-Glu-Val- Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-Leu-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu-Nle-Glu-Ile-Ile-NH₂; or

Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Ala-Arg-Ala-Glu-Gln-CML-Ala-Gln-Gln-Glu-His-D-Ser-Lys-Arg-Lys- Leu-Nle-Glu-CML-Ile-NH₂.

21. (new) A peptide having the formula:

Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val-Leu-Glu-Nle-Thr-Lys-Ala-Asp-Gln-Leu-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys-Leu-Nle-Asp-Ile- Ala-NH₂; or

Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val- Leu-Glu-Nle-
Ala-Arg-Ala-Glu-Gln-CML-Ala-Gln-Gln-Glu-His-Ser-Lys-Arg-Lys- Leu-Nle-Glu-Ile-
Ile-NH₂; or

Ac-Pro-Pro-Ile-Ser-Leu-Asp-Leu-Thr-D-Phe-His-Leu-Leu-Arg-Glu-Val- Leu-Glu-Nle-
Ala-Arg-Ala-Glu-Gln-Leu-Ala-Gln-Gln-Glu-His-Aib-Lys-Arg-Lys- Leu-Nle-Glu-Ile-Ile-
NH₂.